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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/673,575	09/30/2003	Sudhir K. Sinha	P56885	2640

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EXAMINER	
BABIC, CHRISTOPHER M	
ART UNIT	PAPER NUMBER
1637	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/18/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/673,575	SINHA ET AL.	
	Examiner	Art Unit	
	Christopher M. Babic	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5-9 and 21-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5,7,8 and 21-24* is/are rejected.

7)☒ Claim(s) *6* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

Claim(s) 1, 5-9, and 21-24 are pending. The following Office Action is in response to Applicant's response dated February 6, 2007.

Claim Rejections - 35 USC § 102

Applicant's arguments with respect to the rejection(s) of claim(s) 1, 7, and 21 over have been fully considered and are persuasive. Keller does not teach primers drawn to Alu sequences, thus not teaching intra-Alu PCR as defined within the specification. Therefore, the rejection has been withdrawn.

Claim Rejections - 35 USC § 103

Upon further consideration, the rejections of claim(s) 1, 7, 8, and 22 over Sifis in view of Palmirotta have been withdrawn. However, the Examiner continues to maintain that it would have been *prima facie obvious* to amplify an Alu sequence contained exclusively within the human genome within the methods of Sifis, and the new grounds of rejection is made to provide basis for that assertion.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

1. Claim(s) 1, 7, 8, and 21-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sifis et al. ("A more sensitive method for the quantitation of genomic DNA by Alu amplification" J Forensic Sci. 2002 May;47(3):589-92) in view of Palmirotta et al. ("Origin and Gender Determination of Dried Blood on a Statue of the Virgin Mary" Journal of Forensic Science. March 1998. (43) 2, Pages 431-434), in further view of Jurka ("A new subfamily of recently retroposed human Alu repeats" Nucleic Acids Research. 1993. Vol. 21. No. 9, Page 2252) as evidenced by Batzer et al. ("Standardized Nomenclature for Alu Repeats" Journal of Molecular Evolution. 1996. 42, pg. 3-6).

With regard to claim(s) 1, 21, and 22, Sifis teaches a method (pg. 589, 590, materials and methods, for example) comprising: providing a sample to be analyzed (pg. 589, 590, materials and methods, amplification, for example); amplifying predetermined genomic DNA containing an Alu element by using primers (pg. 589, 590, materials and methods, amplification, for example), the amplification being intra-Alu polymerase chain reaction amplification (pg. 589, 590, materials and methods, amplification, for example); and measuring the amount the human DNA by comparing the amplified DNA with a reference (fig. 1, 2; pg. 589, 590, materials and methods, amplification, for example).

With regard to claim 8, Sifis teaches detecting the human DNA using a quantitative PCR system (pg. 590, col. 1, for example).

Sifis further teaches that the assay is based on the amplification of core Alu sequences, i.e. intra-Alu PCR, from primate DNA (pg. 589, 590, materials and methods, amplification, for example). Sifis further highlights that it is desirable that any method of quantitation be **primate specific**; otherwise, any substantial contamination may lead to overestimation of the amount of primate DNA within the sample DNA extract. Sifis does not however, expressly teach the amplification of Alu sequences that are contained exclusively in the human genome.

Palmirotta provides a supporting disclosure that teaches the PCR amplification of Alu sequences for the specific purpose of determining the origin of the DNA (i.e. human DNA or non-human primate DNA) (pg. 432, col. 1, PCR amplification, for example). Palmirotta expressly teaches that PCR-based methods **targeting human Alu**

sequences may contribute to the evaluation of biological samples of suspected human origin (pg. 431, col. 2, para. 4, for example). Thus, it is clear from the teachings of Palmirotta that the amplification of Alu sequences that are not exclusively contained within the human genome, from an unknown nucleic acid sample, can lead to amplification of unwanted primate DNA, e.g. non-human primates DNA.

With regard to claim 7, Palmirotta teaches detecting the human DNA on an agarose gel stained with ethidium bromide (Figure 1).

Thus, Palmirotta does not teach the amplification of Alu sequences that are contained exclusively in the human genome.

Jurka provides a supporting disclosure that teaches the discovery of an Alu, mutation specific, subfamily Sb2 (see reference: Batzer et al. "Standardized Nomenclature for Alu Repeats" Journal of Molecular Evolution. 1996. 42, fig. 1, pg. 3-6, for example) **exclusively contained** within the human genome that is particularly suited for experimental probing (pg. 2252, col. 1, for example). Thus, it is clear from the teachings of Jurka that Alu sequences exclusively contained within the human genome were well known in the art at the time of invention.

Thus, it is asserted that a practitioner of ordinary skill in the art at the time of invention wanting to quantify human DNA from an unknown source through the method of Sifis would have been motivated select an Alu known to reside strictly within the human genome to obtain accurate human results. Thus, it would have been *prima facie obvious* to a practitioner of ordinary skill in the art at the time of invention to practice the methods as claimed.

With regard to claim(s) 23 and 24, it would have been further *prima facie obvious* to a practitioner of ordinary skill in the art at the time of invention to incorporate primers that are complementary to the specific Alu sequence.

2. Claims 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over Sifis et al. ("A more sensitive method for the quantitation of genomic DNA by Alu amplification" J Forensic Sci. 2002 May;47(3):589-92) in view of Palmirotta et al. ("Origin and Gender Determination of Dried Blood on a Statue of the Virgin Mary" Journal of Forensic Science. March 1998. (43) 2, Pages 431-434), in further view of Jurka ("A new subfamily of recently retroposed human Alu repeats" Nucleic Acids Research. 1993. Vol. 21. No. 9, Page 2252) as evidenced by Batzer et al. ("Standardized Nomenclature for Alu Repeats" Journal of Molecular Evolution. 1996. 42, pg. 3-6) as applied to claim(s) 1, 7, 8, 21, and 22 above, and in further view of Buck et al. ("Design Strategies and Performance of Custom DNA Sequencing Primers") BioTechniques. September 1999. 27: Pages 528-536).

Regarding claim(s) 5, the methods of the previously applied references have been outlined in the above rejections. The previously applied references do not expressly disclose the *exact* primer sequences of SEQ ID NO: 3 and SEQ ID NO: 4, drawn to the "young" Yb8 Alu subfamily.

Jurka discloses the entire Sb2 Alu subfamily sequence (fig. 1, for example). The term "Sb2" is considered to be older nomenclature of the "young" Yb8 subfamily (see

reference: Batzer et al. "Standardized Nomenclature for Alu Repeats" Journal of Molecular Evolution. 1996. 42, pg. 3-6, for example).

The *identical* sequence presented in SEQ ID NO: 3 (5'-CGAGGCGGGTGGATCATGAGGT-3' is contained in the sequence provided by Jurka (fig. 1, for example) from nucleotides 48-69. Furthermore, the *identical* complement of the sequence (i.e. reverse primer) presented in SEQ ID NO: 4 (5'-TCTGTCGCCCAGGCCGGACT -3' is contained in the sequence provided by Jurka (fig. 1, for example) from nucleotides 273-254.

Buck provides a supporting disclosure that expressly provides evidence of the equivalence of primers. Specifically, Buck invited primer submissions from a number of labs (39) (pg. 532, col. 3, for example), with 69 different primers being submitted (pg. 530, col. 1, for example). Buck also tested 95 primers spaced at 3 nucleotide intervals along the entire sequence at issue, thereby testing more than 1/3 of all possible 18 mer primers on the 300 base pair sequence (pg. 530, col. 1, for example). When Buck tested each of the primers selected by the methods of the different labs, Buck found that EVERY SINGLE PRIMER worked (pg. 533, col. 1, for example). Only one primer ever failed, No. 8, and that primer functioned when repeated. Further, EVERY SINGLE CONTROL PRIMER functioned as well (pg. 533, col. 1, for example). Buck expressly states "The results of the empirical sequencing analysis were surprising in that nearly all of the primers yielded data of extremely high quality (pg. 535, col. 2, for example)." Therefore, Buck provides direct evidence that all primers would be expected to function, and in particular, all primers selected according to the ordinary criteria, however

different, used by 39 different laboratories. It is particularly striking that all 95 control primers functioned, which represent 1/3 of all possible primers in the target region. This clearly shows that every primer would have a reasonable expectation of success.

Thus, since the claimed primers simply represent complementary functional homologs of the sequences taught by Jurka, the claimed primers are *prima facie* obvious over Jurka in view Buck et al.

3. Claim(s) 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Sifis et al. ("A more sensitive method for the quantitation of genomic DNA by Alu amplification" J Forensic Sci. 2002 May;47(3):589-92) in view of Palmirotta et al. ("Origin and Gender Determination of Dried Blood on a Statue of the Virgin Mary" Journal of Forensic Science. March 1998. (43) 2, Pages 431-434), in further view of Jurka ("A new subfamily of recently retroposed human Alu repeats" Nucleic Acids Research. 1993. Vol. 21. No. 9, Page 2252) as evidenced by Batzer et al. ("Standardized Nomenclature for Alu Repeats" Journal of Molecular Evolution. 1996. 42, pg. 3-6) as applied to claim(s) 1, 7, 8, 21, and 22 above, and in further view of Gelmini et al. ("Quantitative polymerase chain reaction-based homogeneous assay with fluorogenic probes to measure c-*erb*B-2 oncogene amplification" Clinical Chemistry. 1997. 43:5, Pages 752-758).

Regarding claim(s) 9, the methods of the previously applied references have been outlined in the above rejections. The previously applied references do not specifically disclose the practice of a quantitative PCR system such as *Taq*Man.

Gelmini provides a supporting disclosure that teaches the practice of a quantitative PCR system using *Taq*Man chemistry (fig. 1,2,3; table 1; pg. 754, Columns 1,2, for example). Furthermore, they highlight the advantages of using fluorogenic probes in PCR, such as the circumventing of post-PCR product quantitation procedures (pg. 752, col. 2, para. 2, for example).

It would have been *prima facie* obvious to a practitioner ordinary skill in the art at the time of invention to incorporate a quantitative PCR system into the methods of Sifis since Gelmini suggests such a modification for among other reasons, to circumvent post-PCR product quantitation procedures.

Response to Arguments - Claim Rejections - 35 USC § 103

In light of the new ground(s) of rejection, some of Applicant's arguments are rendered moot. However, the following responses are to the remaining relevant arguments.

With regard to Sifis and Palmirotta, Applicant argues that the references fail to show the specificity of their respective Alu PCR methods, adding that long felt but unsolved needs and the failure of Sifis and Palmirotta to correct for these needs, assist in the establishment of nonobviousness. These arguments are not persuasive because the nature of the methods taught by Sifis and Palmirotta did not necessarily require or

even benefit from the amplification of an Alu sequence exclusively contained within the human genome. First, the methods of Palmirotta teach methods of determining the origin of a sample of DNA of unknown origin. Not knowing if the sample was from a non-human primate (e.g. gorilla, chimpanzee, etc.), it would not have been necessarily beneficial to assay an Alu sequence exclusively contained within the human genome. Second, the items swabbed and analyzed within table 3 of Sifis, show samples (e.g. glove, cup, elevator button) that would have very little chance if any of containing non-human primate (e.g. gorilla, chimpanzee, etc.) DNA, i.e. there is very little chance of contaminating non-primate DNA on an elevator button. Thus, it would not have been necessary to assay an Alu sequence exclusively contained within the human genome because there was virtually no chance of inaccurate results due to contaminating non-primate DNA. However, a practitioner of ordinary skill in the art at the time of invention wanting to quantify **strictly** human DNA from an unknown source (e.g. a crime scene) through the method of Sifis would have been motivated select an Alu known to reside strictly within the human genome to obtain accurate human results.

With regard to Buck, Applicant argues that a prior art disclosing the sequence of a certain gene does not automatically make the particular DNA primers amplifying the specific region of the certain gene obvious. This argument is not persuasive because the rejection of claim 5 is based upon Jurka in combination with Buck, who expressly demonstrates the equivalence of primers.

Applicant further argues that Buck does not discuss primers in the PCR context, but only in the sequencing context. This is not persuasive because in both contexts, the

primers function in a similar manner. In both cases, the primers must hybridize to the appropriate site on the target and be capable of extension. Nothing more or less is required of the primer in one situation over the other.

Allowable Subject Matter

As noted previously, claim(s) 6 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

None of the previously applied references teach or suggest the amplification of the AluYd6 subfamily of human specific Alu elements. The sequences presented in SEQ ID NOs: 5 and 6 are novel and unobvious over the prior art.

Conclusion

Claim(s) 1, 5, 7, 8, 9, and 21-24 are rejected.

Claim(s) 6 is objected to.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher M. Babic whose telephone number is 571-272-8507. The examiner can normally be reached on Monday-Friday 7:00AM to 4:00PM.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

4/13/07

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Patent Examiner
AU 1637

KENNETH R. HORLICK, PH.D
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4/16/07